

SBRT. Multimodal imaging for target definition, image guidance techniques utilizing implanted fiducial markers, 4D-CT scanning and respiration management techniques have considerably improved the SBRT.

In general, the approach to metastatic disease has become more aggressive. A number of specialties offer therapies for patients with liver oligo-metastases and a multidisciplinary team approach in the management of these patients is of utmost importance. Radiotherapy may be utilized for a group of patients who cannot be treated by surgery or RFA and the radiation oncologist should therefore be a member of the team.

There is sufficient data demonstration that SBRT can be used in therapy of liver metastases when the constraints to critical tissues such as stomach, bowel and liver are respected, but there is a great need for randomized clinical trials to prove the efficacy of SBRT in treatment of oligo-metastases and for trials to explore the need for systemic therapy along with SBRT. It is therefore strongly encouraged to participate in large multi-institutional randomized trials.

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The role of surgical resection in liver oligo-metastatic disease

P. Naredi¹

¹Sahlgrenska University Hospital, Surgery, Gothenburg, Sweden

When a patient is diagnosed with liver metastases it is by definition a systemic disease and metastases at other sites should also be expected. This is also the case for the third most common cancer disease, colorectal cancer (CRC). Almost half of all patients with CRC will develop liver metastases (CLM) and approximately a fourth of them have only the liver as metastatic site. If the patient has no serious co-morbidities and 30 percent of the liver parenchyma and one hepatic vein can be saved there is indication for liver resection. This is a relative safe procedure with a postoperative mortality below five percent and this subpopulation of patients with CRC has a 5-year survival of 40-50 percent and 30 percent 10-year survival.

The good outcome in liver resected patients is the main reason for follow-up with tumour markers and CT scan after surgery of the primary tumour.

Neoadjuvant chemotherapy will slightly improve progression free survival but not overall survival. Still most patients are today offered neoadjuvant therapy. From a multidisciplinary perspective conversion therapy is important. A majority of patients with CLM will get a response on chemotherapy and they shall then be reconsidered for liver resection. The 5-year survival is as good as for patients who were primarily resectable. On the other hand, patients with CLM that progress on chemotherapy have a bad prognosis, even after liver resection.

From a surgical point of view a patient might have a limited metastatic volume in the liver but one or more small metastases can be badly situated. In this case ablative techniques (radiofrequency or microwave ablation) or stereotactic radiotherapy can be of great value to complement resection of other parts of the liver.

Even if CLM is the most common indication for liver resection of metastatic disease there are other cancer diseases where surgery for oligo-metastatic disease shall be considered. These are primarily neuroendocrine tumours (NET), renal cell cancer, melanoma and ovarian cancer. As with CLM there are no randomised studies to support the indication for surgery but the evidence are generated by comparing survival of liver resected patients with a cohort who had similar tumour burden but were not operated.

SYMPOSIUM: FUNCTIONAL IMAGING FOR RADIOTHERAPY DOSE PAINTING

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Quantitative MR imaging for radiotherapy

W. Foltz¹

¹University of Toronto, Radiation Oncology, Toronto, Canada

Quantitative MRI holds the promise to augment radiotherapy with functional imaging, which may enable improved tumor targeting, and more personalized treatment based on a priori characterization of imaging biomarkers and early assessment of treatment response. This lecture emphasizes some factors of quality, validation, and applications of quantitative MRI metrics.

Diffusion-weighted imaging (DWI) geometric accuracy at 3 Tesla: Geometric accuracy is of fundamental importance for incorporation of anatomic imaging into radiation therapy, yet the geometric accuracy of clinical DWI pulse sequences is under-emphasized. Segmented echo-planar (EPI) DW imaging is an accessible solution on many pre-clinical high-field MRI systems, providing dramatic geometric accuracy

improvement compared to single-shot EPI-DWI at similar scan time and signal-to-noise. Utilizing the RESOLVE works-in-progress package provided by Siemens Medical Systems, segmented EPI DWI has been investigated as an option for more geometrically accurate clinical DWI at 3T. The geometric accuracy improvement from RESOLVE is verified using an in vitro prostate phantom, and applied in vivo to enable tumor-targeted radiation therapy treatment planning for prostate cancer at 3 Tesla based on DWI and T₂-weighted image co-registration (see Figure).

Dynamic contrast enhanced (DCE) MRI validation against DCE-CT: DCE-MRI has broad appeal as a clinical biomarker for radiation oncology, yet presents with known limitations to accuracy and precision. These known limitations apply to both vessel-based measurements of arterial input function (AIF) and tumor-based measurements of permeability and perfusion. Methodologic improvements have been incorporated at 3 Tesla and tested against the standard of DCE-CT. First, a multi-modal DCE-MRI/CT flow phantom has been applied to investigate factors affecting AIFs measured using the MRI magnitude signal, and to validate AIFs measured using the MRI signal phase. Second, a 4D temporal segmentation (TDS) method, which enables voxel-based, parametric analysis based on patient-specific dynamic behaviour of contrast flow, has been implemented to facilitate tissue-level analysis. Preliminary testing has compared DCE-CT supported by 4D-TDS to standard DCE-MRI analysis for the detection of early changes in brain tumor perfusion following radiosurgery.

Stromal imaging: Hedgehog (Hh) pathway inhibition is a potential strategy to overcome treatment resistance and repopulation in patients undergoing radiotherapy and concurrent chemotherapy, and it is now widely held that the Hh pathway promotes tumor growth indirectly through paracrine effects on the stroma. MRI biomarkers to monitor Hh inhibition and stromal depletion have been investigated in murine models of human cervical, pancreatic, and breast cancer, utilizing the 7 Tesla MRI of the STTARR facility, with emphasis on DCE-MRI, magnetization transfer, and DWI.

Figure: A prostate DWI geometric distortion phantom, consisting of distilled water within concentric acrylic cylinders of 3, 6, and 12 cm (e.g. corresponding to the outer diameter of the Hologic endorectal coil diameter; the anterior peripheral zone; and the anterior prostate) was imaged with RESOLVE and standard DWI at 3 T (1.4x1.4x3-mm resolution, 28 slices). (a, b) Meshes of cylinder boundaries for RESOLVE and standard DWI were generated, and cylinder boundaries were tracked to quantify vertical distortion in the phase encoding direction. Compared to standard DWI, RESOLVE reduced the mean RMS displacement of inner and middle cylinders 3-fold (to 0.5 mm) and reduced the maximum distortion in y from 13 to 3 mm. (c-d) clinical prostate RESOLVE and standard DWI ADC maps at 3T in matched slices, verifying distortion reduction in vivo in approximately equivalent scan times and matched spatial resolution (1.4x1.4x3-mm voxels).

